

PCT

WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : A61K 6/06, 6/083, A61L 27/44, C09C 1/00, 3/00		A1	(11) International Publication Number: WO 00/69392 (43) International Publication Date: 23 November 2000 (23.11.00)
(21) International Application Number: PCT/US00/13708			San Antonio, TX 78058 (US). DIXON, Hong [US/US]; 11417 Lago Vista, Helotes, TX 78023 (US).
(22) International Filing Date: 19 May 2000 (19.05.00)			(74) Agent: MORRIS, Paula, D.; Paula D. Morris & Associates, P.C., 2925 Briarpark Drive, Suite 930, Houston, TX 77042-3728 (US).
(30) Priority Data: 09/314,350 19 May 1999 (19.05.99) US			(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
(63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US 09/314,350 (CIP) Filed on 19 May 1999 (19.05.99)			
(71) Applicants (for all designated States except US): SOUTHWEST RESEARCH INSTITUTE [US/US]; 6220 Culebra Road, San Antonio, TX 78238-5166 (US). UNIVERSITY OF TEXAS SYSTEM [US/US]; 201 West 7th Street, Austin, TX 78701-2981 (US).			
(72) Inventors; and (75) Inventors/Applicants (for US only): FURMAN, Benjamin, R. [US/US]; 6338 Rustling Lane, San Antonio, TX 78249 (US). RAWLS, Henry, R. [US/US]; 340 Argo Avenue, San Antonio, TX 78209 (US). NORLING, Barry, K. [US/US]; 13427 Shorecliff Street, San Antonio, TX 78248 (US). WELLINGHOFF, Stephen, T. [US/US]; 7718 Benbrook,			Published With international search report. With amended claims.
(54) Title: MECHANICALLY STRONG AND TRANSPARENT OR TRANSLUCENT COMPOSITES MADE USING ZIRCONIUM OXIDE NANOPARTICLES			
(57) Abstract			
<p>Metal oxide nanoparticles having at least some surface acid sites functionalized with an adhesion promoter and at least some surface acid sites functionalized with a coupling agent. The nanoparticles are useful in forming composites comprising photopolymerizable matrix monomers, and are primarily suitable for dental and medical restoration. In a preferred embodiment, the metal oxide comprises zirconium, and the coupling agent is a zirconate.</p>			

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

MECHANICALLY STRONG AND TRANSPARENT OR TRANSLUCENT COMPOSITES MADE USING ZIRCONIUM OXIDE NANOPARTICLES

The present invention relates to metal oxide particles functionalized with a mobile adhesion promoter to increase hydrophobicity and functionalized with an amount of a coupling agent effective to copolymerize with monomers in a matrix resin to form a strong, translucent or transparent composite. In a preferred embodiment, the metal oxide particles are zirconium oxide particles, the mobile adhesion promoters are silanes, and the coupling agents both are zirconates. The composites are primarily suitable for dental and medical restoration; however, optical resins for use in high refractive index applications such as eyeglasses, resins for advanced prototyping, and adhesive applications also are possible.

Background of the Invention

Colloidal fumed silica nanoparticles currently are used as fillers in "microfilled" composite dental restorative resins. These particles can increase the hardness and wear resistance of photocured matrix polymers; however, the particles are not radiopaque and cannot be homogeneously dispersed within the matrix resin because of interparticle associations. The resulting coagulation leads to a substantial increase in viscosity and a consequent decrease in composite workability. This places a severe limitation on the practical filler loading in "microfilled" composites.

The loading problem can be partially offset by incorporating prepolymerized organic fillers into the resin in which a relatively high level of colloidal silica is incorporated into highly crosslinked polymeric granules. The workability of the composite resins containing these fillers is maintained, and the cure shrinkage is

somewhat reduced. However, the fillers also yield failure prone interfaces and cause a high degree of light scattering, thereby limiting the depth of cure.

Photocurable dental repair materials are needed which are transparent or translucent, radioopaque, have good workability, and have good mechanical strength and 5 stability. The use of metal oxides as fillers in such materials results in transparent or translucent, radioopaque materials. However, the hydroxyl groups that tend to form at the surface of metal oxide particles in "protic" environments tend to make the surface of the particles hydrophilic. As a result, the metal oxide particles have difficulty being wetted or adhered to by relatively hydrophobic matrix monomers, such as acrylic monomers, 10 which are non-polar or only weakly polar in nature.

Summary of the Invention

The invention provides metal oxide particles comprising a surface functionalized with an amount of an adhesion promoter and with a quantity of an organofunctional coupling agent. The invention also provides polymerizable mixtures comprising these 15 particles and the resulting, polymerized composites.

Detailed Description of the Invention

The present invention is directed to functionalized metal oxide clusters, both alone and combined with a resin comprising matrix monomers copolymerizable with functionalities on the clusters. The resin has good workability, and forms a composite 20 which is mechanically strong and stable. Preferred functionalized metal oxide particles comprise zirconium oxide clusters functionalized with a polymerizable coupling agent and an adhesion promoter.

Substantially any "metal" capable of forming an amphoteric metal oxide may be used to form the metal oxide particles. Suitable metallic elements include, but are not

necessarily limited to niobium, indium, titanium, zinc, zirconium, tin, cerium, hafnium, tantalum, tungsten, and bismuth. Also suitable in place of the metal in the oxide is the semi-metallic compound, silicon. As used herein, unless otherwise indicated, the term "metal oxide" is defined to include silicon, and the word "metal," when used to refer to 5 the metal oxide is intended to also refer to silicon.

The metal oxides may be made of a single metal, or may be a combination of metals, alone or combined with other impurities or "alloying" elements, including, but not necessarily limited to aluminum, phosphorus, gallium, germanium, barium, strontium, yttrium, antimony, and cesium. Binary and tertiary compounds may be more easy to 10 silanate, and may be produced by mixing precursors containing different metal or semi-metal groups. Preferred metal oxide particles comprise zirconium oxide. Alternately, it may be preferable to use zirconium silicate particles (commonly known as "zircon"), as zircon is easier to silanate than zirconium.

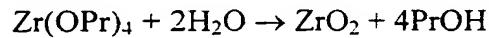
The metal oxide nanoparticles may be prepared using any known methods, such 15 as "sol-gel" techniques, direct hydrolysis of metal alkoxides by water addition, forced hydrolysis of relatively low-cost metal salts, or non-hydrolytic reactions of metal alkoxides with metal halide salts. Examples of such procedures are shown in the following references, each of which is incorporated herein by reference: W. Stöber and A. Fink, *J. of Colloid and Interface Science*, v. 26, 62-69 (1968); M.Z.-C. Hu, M.T. 20 Harris, and C.H. Byers, *J. of Colloid and Interface Science*, v. 198, 87-99 (1988); M. Ocaña and E. Matijević, *J. of Materials Research*, v. 5(5), 1083-1091 (1990); L. Lerot, F. LeGrand, P. de Bruycker, *J. of Materials Science*, v. 26, 2353-2358 (1991); H. Kumazawa, Y. Hori, and E. Sada, *The Chemical Eng'g. Journal*, v. 51, 129-133 (1993); S. K. Saha and P. Pramanik, *J. of Non-Crystalline Solids*, v. 159, 31-37 (1993); M.

Andrianainarivelo, R. Corriu, D. Leclercq, P.H. Mutin, and A. Vioux, *J. of Materials Chemistry*, v. 6(10), 1665-1671 (1996); F. Garbassi, L. Balducci, R. Ungarelli, *J. of Non-Crystalline Solids*, v. 223, 190-199 (1998); J. Spatz, S. Mössmer, M. Mo[umlaut]ller, M. Kocher, D. Neher, and G. Wegner, *Advanced Materials*, v. 10(6), 473-475 (1998); R. F. 5 de Farias, and C. Airoldi, *J. of Colloid and Interface Science*, v. 220, 255-259 (1999); T. J. Trentler, T. E. Denler, J. F. Bertone, A. Agrawal, and V.L. Colvin, *J. of the Am. Chemical Soc.*, v. 121, 1613-1614 (1999); Z. Zhan and H.C. Zheng, *J. of Non-Crystalline Solids*, v. 243, 26-38 (1999); M. Lade, H. Mays, J. Schmidt, R. Willumeit, and R. Schomäcker, *Colloids and Surfaces A: Physicochemical and Eng'g Aspects*, v. 163, 3-15 10 (2000); and the procedure described in "Sol-gel processing with inorganic metal salt precursors," authored by "Michael" Zhong Cheng Hu, licensable via Oak Ridge National Laboratory under ORNL control number ERID 0456.

A preferred method of forming the metal oxide nanoparticles is water hydrolysis of corresponding metal alkoxides, preferably normal metal alkoxides having from about 1 15 to about 4 carbon atoms per hydrolyzable group. Where the metal used is zirconium, a preferred zirconium alkoxide for use in this procedure is zirconium propoxide. Although the following description is couched in terms of preparing zirconium oxide particles, the description applies equally to the preparation of other metal oxide nanoparticles.

If desired, the cluster synthesis may be enhanced using a suitable acid, preferably 20 formic acid, as described in U.S. Patent No. 5,372,796 to Wellinghoff, incorporated herein by reference. Hydrolysis without using formic acid enhancement preferably takes place in the presence of excess alcohol as a diluent, preferably ethanol or propanol, most preferably n-propanol, in the presence of an inert gas, preferably nitrogen gas. Small droplets of water for hydrolyzing the zirconium alkoxide preferably are progressively

added to the solution while stirring. The water droplets also preferably are diluted to a concentration of from about 1% (w/w) to about 3% (w/w) in a lower alcohol having from about 1 to about 3 carbon atoms, preferably propanol. In order to fully hydrolyze the zirconium alkoxide, the amount of water added must be twice the molar amount of the zirconium alkoxide unless the hydrolysis is enhanced using formic acid. During the addition of the water droplets, the solution is stirred vigorously. Typically, the addition of acid to produce a pH of about 3 is sufficient to form an adequate dispersion of zirconia clusters. Substantially any acid having a pH of less than about 3 may be used for this purpose, suitable acids including but not necessarily limited to nitric acid, hydrochloric acid, sulfuric acid, and the like. The chemical stoichiometry is as follows:



In a preferred embodiment, a suitable organic acid is used to increase the rate of hydrolysis and to increase the amount of positive surface charge on the resulting zirconia clusters while producing only volatile byproducts. Any organic acid may be used as long as the ester resulting from the reaction has a low vapor pressure such that the ester will evaporate below about 200°C. In this embodiment, an amount of acid (preferably concentrated formic acid) which is about 1 to about 2 times the molar quantity of the alkoxide is added to the solution after adding the water/alcohol mixture. The solution is stirred for a prolonged period of from about 1 hour to about 24 hours, preferably about 12 hours. The reaction proceeds as follows:



When formic acid is used, the resulting clusters tend to grow large enough to scatter visible light, thereby giving the stirred solution a milky white appearance. If a smaller average cluster size is desired, then the system may be further acidified to a pH of

near 1 by adding a strong acid, such as hydrochloric or nitric acid, in order to partially digest the clusters. The solution is stirred until achieving a desired average cluster size, preferably from about 20 nm to about 100 nm. The cluster size is measured using transmission electron microscopy (TEM), atomic force microscopy (AFM), or simple 5 visual inspection based upon known light scattering phenomena.

Assuming perfect bonding between the particle and matrix, a decrease in particle size at a given volume fraction of particles will increase the elastic constraint on the deforming matrix molecules and lead to an increase in modulus. However, as the particle size approaches molecular dimensions, the very closely spaced crosslinking points of high 10 functionality within the matrix will substantially quench any large scale molecular motions. It is these motions which are important for energy dissipation and fracture toughness.

In order to accommodate both factors, the particles preferably are "nanoparticles," or particles having an average "diameter in nanometers" defined herein as from about 10 15 nm to about 150 nm, preferably about 50 to about 100 nm. The desired average diameter in nanometers is small enough to provide sufficient transparency for photopolymerization but large enough to provide effective fracture toughness after photopolymerization. In other words, the average diameter in nanometers permits the material to be effectively cured by photopolymerization and also provides effective fracture toughness after curing.

20 Once the desired average cluster size is achieved through adjustment of the solution pH, the clusters are organofunctionalized with an organofunctional coupling agent. The ideal organofunctional coupling agent readily and irreversibly condenses with the surface of the metal oxide clusters and also provides a polymerizable functionality, preferably a double bond functionality, to the clusters to permit the clusters to

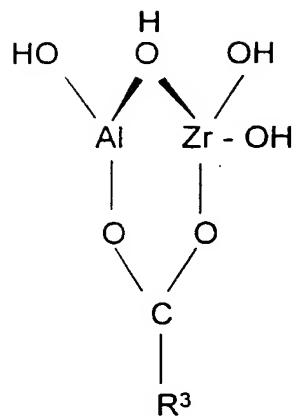
copolymerize with a suitable surrounding organic matrix resin. The organofunctional coupling agents also preferably render the clusters more hydrophobic.

Suitable organofunctional coupling agents include polymerizable groups, including, but not necessarily limited to photopolymerizable groups such as vinyl, acryl, 5 epoxy, or methacryl groups. Examples include, but are not necessarily limited to mono-, di-, and tri-functional silanes, isocyanates, zirconates, aluminozirconates, zirconyl methacrylate, titanates, and phosphonates. Preferred organofunctional groups, which increase the hydrophobicity of the clusters and also maximize the mechanical strength of the resulting composite are hydrolyzable zirconates having the following general 10 structure:



wherein R^1 is selected from the group consisting of hydrolyzable alkyl groups and hydrolyzable alkenyl groups having 1 or more carbon atoms, said alkyl groups being effectively eliminatable from the system as free molecules either by volatilization or by 15 isolated copolymerization within the organic matrix resin, and R^2 is selected from the group consisting of copolymerizable alkenyl substituents containing 2 or more carbon atoms. R^1 generally may be eliminated by volatilization if the number of carbon atoms is less than 9. Preferred organofunctional groups are neopentyl (diallyl) oxy trimethacryl zirconates and neopentyl (diallyl) oxy triacryl zirconates (described in U.S. Patent No. 20 4,623,738, incorporated herein by reference).

Aluminozirconates having the following general structure also are preferred as organofunctional groups for zirconia clusters:

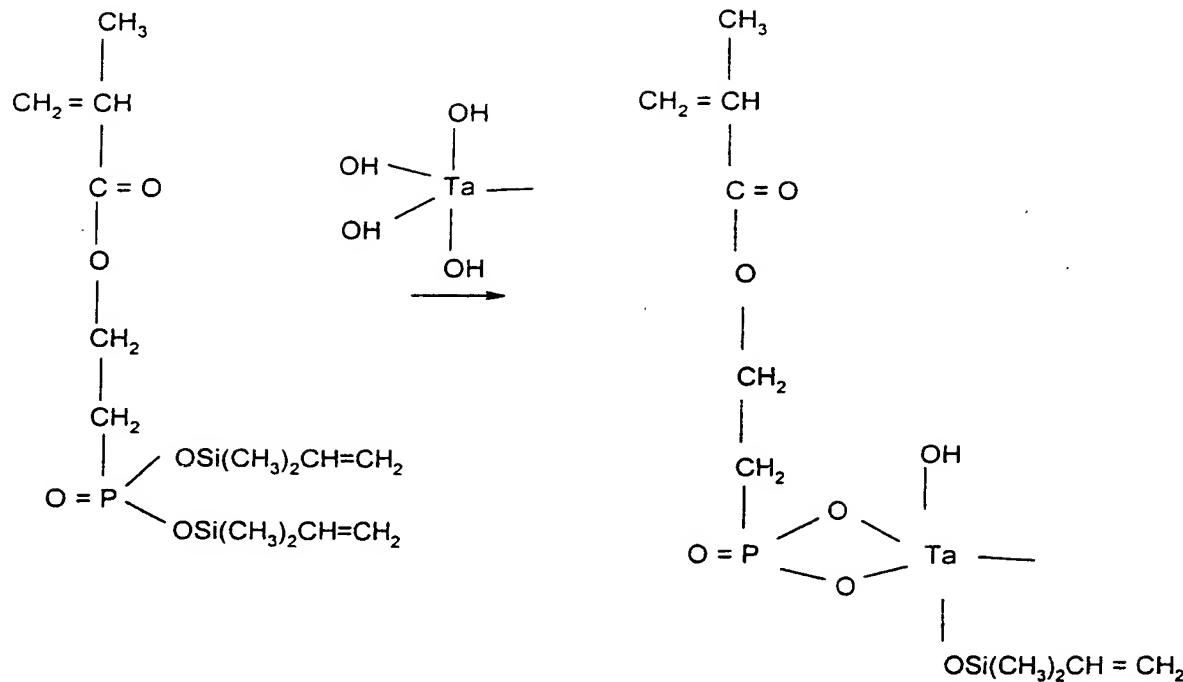


wherein R^3 is selected from the group consisting of copolymerizable alkenyl groups and carboxyfunctional substituents containing 1 or more carbon atoms, respectively.

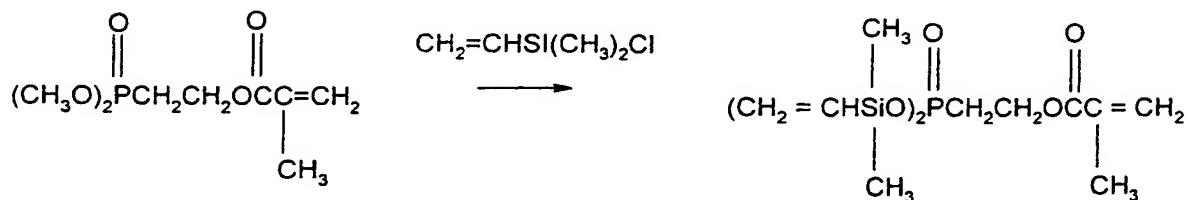
Preferred aluminozirconates are methacryloxy aluminozirconates (described in U.S.

5 Patent Nos. 4,539,049 and 4,539,048, both of which are incorporated herein by reference).

In another preferred embodiment, the polymerizable functionality is reacted with the oxide surface through a phosphonate linkage, which has good hydrolytic stability and will react with the metal-OH bonds only through the ester bonds, as shown below:

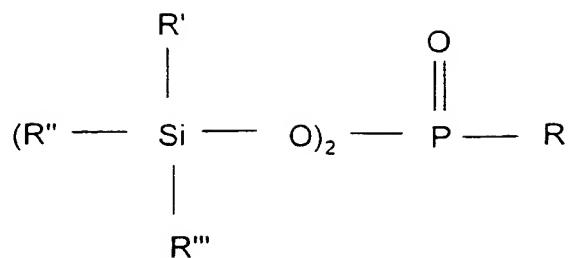


In order to make an especially active phosphonating species, the dimethyl ester of methacryl phosphonate was reacted with a silanating agent to form the hydrolytically unstable vinyl dimethyl silyl ester. The silanating agent can be a chloride, as shown below, or a bromide.



10 This reaction is quite generic and can be used to form any trialkylsilyl ester (e.g., trimethylsilyl) of any functionalized phosphonate, including vinyl phosphonate. Suitable esters have the general formula:

10

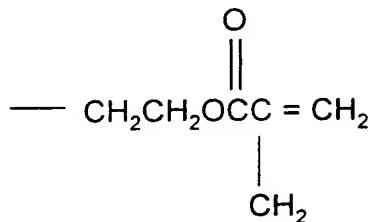


wherein R is a polymerizable group, such as a vinyl, acryl, or methacryl group, and R', R'', and R''' are the same or independently selected from the group consisting of 5 alkyl groups and alkenyl groups.

For example, in addition to the trialkyl silyl ester of vinyl phosphonate, phosphonates having the following groups can be used:

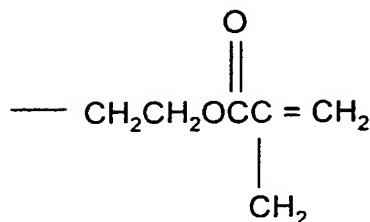
1. R is -CH=CH₂ and R', R'', and R''' each are -CH₃ groups;
2. R is

10



and R', R'', and R''' are each -CH₃; and

3. R is



15

and R¹, R² and R³ are each -CH₃; and

R³ is CH₂=CH₂

The silyl phosphonate esters can serve two purposes. One purposes is as a surface phosphinating agent, and the other as a surface silanating agent which will generate the

5 hydrophobic surface necessary for incorporation into hydrophobic monomers. If the silane is alkene functionalized, or otherwise functionalized with a polymerizable functionality, then the silane also acts as a coupling agent via the phosphonating agent.

The phosphonating agent may be incorporated into the metal oxide particles using any acceptable means. The phosphonating agent conveniently is incorporated by ester 10 exchange of the metal ethoxide with an acid, such as formic acid. Alternately, the metal oxide prepared using conventional means may be exposed, preferably in an alcohol solution, to the silyl phosphonate and trifunctional silane. Any other suitable incorporation method is acceptable.

Even though a given metal oxide cluster may have experienced extensive 15 phosphonating and silanating, the infrared spectrum still indicates the presence of a substantial amount of Ta-OH. The remaining accessible Ta-OH may be further reduced by adding a trifunctional silane, such as 3-(trimethoxysilyl) propyl methacrylate to the formic acid mixture. This component also is useful since the multiple Ta-O-Si bonds formed by the trifunctional silane are more hydrolytically stable than the monofunctional 20 silanes. In addition, the silane effectively blocks access to unreacted Ta-OH bonds. Thus, interparticle hydrogen bonding associations between Ta-OH bonds on adjacent particles is blocked and premature phase separation of a tantalum rich phase in the hydrophobic matrix monomer is avoided.

The required amount of organofunctional coupling agent may vary from about 0.01 to about 0.3 times the molar content of the metal oxide, preferably zirconium oxide, in the ceramer. Quantities on the order of 0.2 times the molar content of zirconium oxide have been used to produce strong ceramers using dimethacrylate resins.

5 In order to organofunctionalize the clusters, the coupling agents are diluted with an excess of a suitable diluent, preferably an alcohol having from about 1 to about 4 carbon atoms, most preferably propanol, and added to the alcohol-zirconia-cluster solution. It is beneficial to maintain the acidity of the solution at a pH of from about 1 to about 3, preferably at about 3, in order for the reaction between the zirconia clusters and 10 the primary coupling agent to be both timely and effective. The acidity may be maintained by adding a suitable inorganic acid, such as nitric acid. The resulting solution is agitated, preferably by stirring, for a prolonged period of time, preferably at room temperature or ambient temperature, in order to accomplish the organofunctionalization. A typical stirring time is about 3 days.

15 After the primary organofunctionalization has taken place, the zirconia clusters may be left in the alcohol solution for further treatment. Alternately, if the solids yield is to be assessed, the clusters may be dried by vacuum evaporation, weighed, and the clusters may be redissolved in one of the lower alcohols, preferably methanol, at a later time. In either case, it is preferable to form stable complexes or bonds between a 20 secondary, highly mobile adhesion promoter and a quantity of those hydroxyl groups not complexed to the coupling agent in order to further compatibilize the metal oxide clusters with the relatively hydrophobic resin. The quantity of hydroxyl groups complexed with the mobile adhesion promoter should be sufficient to displace as many hydroxyl groups from the zirconia surfaces as possible and then to remain in place long enough to allow

the particles to be homogeneously dispersed in a highly hydrophobic resin. This typically requires complexation or bonding with about 50% or more of the hydroxyl groups.

Preferred "mobile adhesion promoters" are defined as surface-active molecules which strongly bind to the surface of the metal oxide cluster, preferably via primary 5 chemical bonding. In a preferred embodiment, the polar end of the surface-active molecule preferably is bound to the surface by displacing the hydrogen of a hydroxyl group. The hydrophobic tail of the mobile adhesion promoter may intertwine with, but preferably does not chemically react with molecules in the matrix resin. Suitable mobile adhesion promoters include, but are not necessarily limited to silanes, phosphonates, 10 phosphates, chelating agents, such as acetylacetone, fatty acids, such as stearic acid, fatty alcohols, and ester linked fatty acids. Preferred mobile adhesion promoters are silanating agents.

Preferred silanating agents are silanes bearing substituents selected from the group consisting of: from about 1 to about 3 alkyl groups having from about 1 to about 18 15 carbon atoms; from about 1 to about 3 alkenyl groups; and, from about 1 to about 3 substituents selected from the group consisting of chlorine, bromine, and an alkoxy group having from about 1 to about 4 carbon atoms. Preferred silanating agents have substituents selected from the group consisting of: one alkenyl group; two alkyl groups having from about 1 to about 3 carbon atoms; and, one alkoxy group having from about 1 20 to about 3 carbon atoms. A most preferred secondary surface agent is dimethyl ethoxy vinyl silane (DMEOVS) (U.S. Patent No. 4,504,231, incorporated herein by reference). DMEOVS has the benefit of increasing the double bond density of the cluster surfaces while also being volatile enough that excessive amounts can be easily removed from the system. Nevertheless, the agent's greatest value is its ability to displace as many

hydroxyl groups from the zirconia surfaces as possible and then to remain in place long enough to allow the particles to be homogeneously dispersed in a highly hydrophobic resin.

Any existing acid in the system will stabilize the silane against oligomerization 5 and will catalyze its reaction with the cluster surfaces. Therefore, it is preferable to further acidify the solution to a pH of from about 1 to about 2, preferably to about 2, by adding a suitable inorganic acid, such as nitric acid. The resulting solution is again agitated, preferably by stirring at ambient conditions, for a prolonged period of time, typically from about 4 days to about 2 weeks.

10 Once the secondary coupling agent has been given sufficient time to react with the surface of the metal oxide, preferably at least 4 days, any acid (such as HCl) remaining in the solution may be removed by an acid scavenger. Any insoluble portion (generally less than 10% by weight) is removed by centrifugation, and any free protons in solution (i.e. HCl) is scavenged. Substantially any suitable acid scavenger may be used, such as 15 polyamines and their copolymers. A preferred acid scavenger is polyvinyl pyridine. Using this acid scavenger, the system pH is adjusted upward to at least about 5, but not more than about 6. The supernatant solution is postreacted with a large excess of the secondary surface active agent in order to displace any hydroxyl groups remaining on the particle surfaces. If clouding of the solution occurs during postreaction, it may be 20 desirable to centrifuge a second time and postreact again with an excess of the secondary surface active agent.

The functionalized nanoparticles then are ready to be mixed with the matrix monomers. Any transparent monomer comprising functional groups polymerizable with the coupling agent on the metal oxide clusters may be used. Suitable functional groups

include, but are not necessarily limited to vinyl, acryl, epoxy, or methacryl groups. For dental applications, methacryl and acryl groups are preferred.

Generally, a solution of from about 10 wt% to about 30 wt% of zirconium oxide nanoparticles in lower alcohol, preferably methanol, is mixed with a solution of a suitable 5 matrix monomers. It is possible that a higher wt% of zirconium oxide nanoparticles also may be used. Suitable matrix monomers include, but are not necessarily limited to glycerol monomethacrylate, glycerol dimethacrylate, hydroxyethylmethacrylate (HEMA), 2,2-bis[p-(2'-hydroxy-3'-methacryloxypropoxy)phenylene]propane ("Bis-GMA), or ethoxylated bis-GMA and various blends of these monomers in combination with known 10 viscosity reducers and photoinitiators or photoactivators. Known viscosity reducers include, but are not necessarily limited to triethyleneglycol dimethacrylate, and polypropylene oxide monomethacrylate. Known photoinitiators and photoactivators include, but are not necessarily limited to camphorquinone and 2-n-butoxyethyl-4-(dimethylamino)benzoate.

15 Since dimethacrylate resin monomers are soluble in the lower alcohols, it is convenient to add these resins directly to the existing zirconia solution, mixing them thoroughly. This liquid state mixing approach assures that all particles have sufficient opportunity to intimately adhere to the resin monomers. Once the mixture becomes homogeneous, the volatile agents may be directly removed by vacuum evaporation, 20 yielding a single phase composite resin. Alternately, the resulting polymer may be isolated by filtration and/or centrifugation. If the hydroxyl groups at the surface of the zirconia clusters are thoroughly displaced, the zirconia clusters will not tend to interact with one another or agglomerate, even at near-neutral pH, once incorporated into a

hydrophobic resin. Experimental samples contained 10, 20 and 30 wt% nanoparticle loadings.

The hydrophobicity of the nanoparticle can be increased by increasing the number of functionalized Zr-OH bonds. The ability to alter the surface of the nanoparticle in a controlled manner permits control of the working time of the unpolymerized composite and modification of the cured microphase structure of the composite material.

For example, if a hydrophobic, matrix monomer and hydrophilic nanoparticles are dissolved in a common hydrophilic solvent, evaporation of the solvent will yield an initially mobile fluid which rapidly will phase separate to form an elastic gel. Elastic properties are generated by an interpenetrating network phase of hydrophilic metal oxide nanoparticles within the hydrophobic matrix. If, on the other hand, the hydrophobic matrix monomer and the relatively hydrophobic nanoparticles are mixed in a common solvent and the solvent is evaporated, microphase separation will proceed more slowly providing increased working or storage time in the mobile state. With increased working time, the kinetic development of phase separation can be terminated at different stages by polymerization of the matrix monomer or prepolymer. Interconnectedness of the oxide network can have a strong influence on mechanical, permeability and electrical properties of the material.

By appropriate matching of the surface properties of the nanoparticles and the matrix monomer, it is possible to make a one phase system or generate a very fine phase separation that is insufficient to scatter light to a depth of at least about 1 millimeter, preferably to about 2 millimeters or more. This is of specific importance in many applications because several millimeters in thickness of such a material can be uniformly

photocured to a solid. In addition, opacifying particles can be added to the transparent base for control of cosmetic features.

The invention will be better understood with reference to the following examples, which are set forth for purposes of illustration only:

5

Example 1. ZrO₂ Cluster Synthesis by Aqueous Hydrolysis

A solution of 10.8367 g of 70% (w/w) zirconium propoxide in propanol was added to a round-bottom flask under nitrogen gas reflux to yield 2.32×10^{-2} moles of the pure alkoxide. The solution was diluted by further adding 60 ml normal propanol while stirring with a magnetic stir bar. To completely hydrolyze the alkoxide, the amount of water added was twice the molar amount of zirconium propoxide, i.e. 4.63×10^{-2} mole. 10 0.84 ml water was diluted with 40 ml normal propanol, and this solution was added to the flask dropwise (by burette) while stirring vigorously. The solution gradually became cloudy as the water was added. In order to increase the rate of hydrolysis, the solution 15 was slightly acidified by adding 0.16 ml concentrated nitric acid to the flask. The solution clarified somewhat, remaining slightly hazy. Stirring was continued for about 2 hours. 2.3 ml (-4.63×10^{-2} mol.) of pure neopentyl(diallyl) methacryl zirconate was diluted in 10 ml propanol and the resulting solution was added to the flask dropwise (by pipette), and the solution was stirred for 2 more hours. The system was then further 20 acidified by adding 0.9 ml concentrated nitric acid, resulting in a system pH of about 3. Stirring was continued for about 3 days.

After stirring for 3 days, the flask was evacuated by pumping until only a dry powder remained. The powder was weighed and determined to have a mass near 6.3 g. The powder then was dissolved in methanol with the aid of a vortex mixer until the solids 25 concentration was in the range of 10-20% (w/w). 15.3 ml (-9.26×10^{-2} mol.) of pure

dimethyl ethoxy vinyl silane was added to the solution. To prevent polymerization of the silane over time, the solution was further acidified by adding 0.7 ml concentrated nitric acid, resulting in a system pH of about 2. Stirring was continued for one week, and the solution was then neutralized with about 5 g polyvinyl pyridine (2% crosslinked) such 5 that the system pH was greater than 5 but no more than 6. The polymeric base was isolated by filtering the solution.

Once the powder has been solvated, cluster concentration is known and is assumed to remain constant during neutralization. This assumption has been confirmed by re-drying aliquots of the solution. Any and all dilutions preferably are recorded.

10 Example 2. ZrO₂ Cluster Synthesis Enhanced by Formic Acid

10.3540 g of 70%(w/w) zirconium propoxide solution was added to a round-bottom flask under nitrogen gas reflux. The solution was diluted with 60 ml normal propanol while stirring with a magnetic stir bar. 0.4 ml water was diluted in 20 ml 15 normal propanol, and this solution was added to the flask dropwise (by burette) while stirring vigorously. The solution became slightly cloudy after the water was added. Stirring was continued for approximately 12 hours, and 1.25 ml concentrated formic acid was added. The resulting solution was stirred for at least 30 minutes, and then 2 ml 20 concentrated hydrochloric acid was added, reducing the system pH to nearly 1. Once the solution was clarified to the point of being only slightly hazy, 2.2 ml of pure neopentyl(diallyl) methacryl zirconate was diluted in 10ml propanol and added to the flask dropwise (by pipette). Stirring was continued for at least 2 hours, and the solution was pump vacuum dried to a powder.

The resulting powder was dissolved in methanol with the aid of a vortex mixer 25 until the solids concentration was in the range of 10-20%(w/w). 14.6 ml of pure dimethyl

ethoxy vinyl silane was added to the solution and the solution was stirred for one week. 4-5 g polyvinyl pyridine (2% crosslinked) was added while monitoring the system pH until it was between 5 and 6. The polymeric base was isolated by centrifugation.

Example 3. Composite Formation Using Zirconia Clusters

5

14.7783 g of a solution having a concentration of clusters of 10.15%(w/w) was added to a round-bottom flask, yielding 1.50 g clusters. Added to this solution, and mixed thoroughly, was 6.00 g of a blend of 37 wt% bis-GMA, 25 wt% tetra ethylene glycol dimethacrylate (TEGDMA), 37.5 wt% bis-EMA (an ethoxylated version of bis-GMA) with 0.2% camphorquinone and 0.3% 2-n-butoxyethyl-4-(dimethylamine)benzoate (CQ/amine) (photoinitiator for on-demand polymerization).

10

The flask was evacuated after mixing in order to remove the volatile methanol and silane from the system. The yield was 7.50 g of composite resin having a solids content of 20%(w/w). The mechanical properties (± 1 standard deviation) of a variety of composite specimens prepared as indicated are given in the Table below:

15

The resin had a fluid consistency which was easily manually packed into transparent silicone molds in order to produce mechanical testing specimens for flexural and fracture toughness testing. Once filled, the specimen molds were centrifuged to aid in the removal of air bubbles prior to photocuring. Specimens were spot cured using a dental curing lamp ($\lambda = 470$ nm, QHL 75, Dentsply) for a minimum of one minute at each location. The flexure specimens were 2.5 x 2.5 x 25 mm in size while the fracture toughness specimens were 8 mm square and less than 4 mm thick. The geometry and testing approach was taken from the ASTM E399 specification, although the specimen size is somewhat smaller than that recommended. The cured specimens were tested to failure, and the fracture surfaces were analyzed by optical microscopy.

Mechanical Property	Unfilled Model Resin	70% Silica-Filled Model Resin	20% Zirconia Filled Model Resin (Formic Acid Used)	20% Zirconia-Filled Model Resin (Inorganic Acid Used)
Breaking Stress (psi)	15271.66 ± 1,695.98	18658.58 ± 2,185.93	38522.47 ± 1,804.53	21816.34 ± 1,995.32
Flexural Modulus (GPa)	2.36 ± 0.21	7.87 ± 0.53	15.73 ± 1.93	12.80 ± 1.08
Fracture Toughness [ksi(in ^{1/2})]	0.4557 ± 0.0436	0.3711 ± 0.2033	0.4586 ± 0.0979	--

Preliminary TEM images revealed that the average particle size was probably much smaller than the expected ~ 100 nm value, which was consistent with the high optical transparency of the sample. The average flexural strength of the resins was as 5 much as 251.8 MPa. The elastic modulus of the materials was as much as 15.73 GPa. The fracture toughness did not deteriorate with filler loadings up to 30 wt%.

Many modifications and variations may be made to the embodiments described herein without departing from the spirit of the present invention. The embodiments described herein are illustrative only should not be construed as limiting the scope of the 10 present invention.

We claim:

1 1. Metal oxide particles comprising a surface functionalized with an amount
2 of a mobile adhesion promoter and with a quantity of an organofunctional coupling agent.

1

1 2. The metal oxide particles of claim 1 wherein the organofunctional
2 coupling agent also comprises an adhesion promoter.

1

1 3. The metal oxide particles of any of claims 1 and 2 wherein the metal oxide
2 comprises a metal selected from the group consisting of niobium, indium, titanium, zinc,
3 zirconium, tin, cerium, hafnium, tantalum, tungsten, bismuth, silicon and combinations
4 thereof.

1

1 4. The metal oxide particles of any of claims 1-3 wherein said metal oxide
2 comprises a metal selected from the group consisting of niobium, indium, titanium, zinc,
3 zirconium, tin, cerium, hafnium, tantalum, tungsten, bismuth, and combinations thereof.

1

1 5. The metal oxide particles of any of claims 1-4 further comprising an
2 alloying element selected from the group consisting of aluminum, phosphorus, gallium,
3 germanium, barium, strontium, yttrium, niobium, antimony, cesium, and combinations
4 thereof.

1

1 6. The metal oxide particles of any of claims 1-5 wherein said metal oxide
2 comprises zirconium oxide.

1 7. The metal oxide particles of any of claims 1-6 wherein said metal oxide
2 comprises zirconium silicate.

1

1 8. The metal oxide particles of any of claims 1-7 further comprising a
2 mixture comprising a matrix resin comprising monomers comprising functional groups
3 polymerizable with said organofunctional coupling agents.

1

1 9. The metal oxide particles of claim 8 comprising an average diameter
2 effective to permit curing of said mixture by photopolymerization.

1

1 10. The metal oxide particles of any of claims 1-9 wherein the amount of the
2 mobile adhesion promoter is effective to disperse the particles in a hydrophobic resin.

1

1 11. The metal oxide particles of any of claims 1-10 wherein the quantity of the
2 or the organofunctional coupling agent is effective to provide fracture toughness after
3 curing.

1

1 12. The metal oxide particles of any of claims 1-11 wherein the
2 organofunctional coupling agent comprises a polymerizable group selected from the
3 group consisting of one or more vinyl groups, acryl groups, epoxy groups, or methacryl
4 groups.

1

1 13. The metal oxide particles of any of claims 1-12 wherein the
2 organofunctional coupling agent comprises a functionality selected from the group

3 consisting of mono-, di-, and tri-functional silanes, isocyanates, zirconates,
4 aluminozirconates, zirconyl methacrylate, titanates, and phosphonates.

1

1 14. The metal oxide particles of any of claims 1-13 wherein the
2 organofunctional groups are hydrolyzable zirconates having the following general
3 structure:



5 wherein

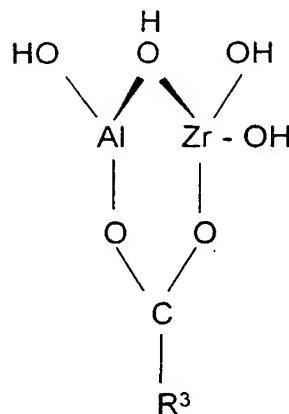
6 R^1 is selected from the group consisting of hydrolyzable alkyl groups and
7 hydrolyzable alkenyl groups having 1 or more carbon atoms; and

8 R^2 is selected from the group consisting of copolymerizable alkenyl substituents
9 containing 2 or more carbon atoms.

1 15. The metal oxide particles of claim 14 wherein R^1 is selected from the
2 group consisting of alkyl groups having from about 1 to about 9 carbon atoms.

1

1 16. The metal oxide particles of any of claims 1-15 wherein the
2 organofunctional groups comprise moieties selected from the group consisting of
3 neopentyl (diallyl) oxy trimethacryl zirconates, neopentyl (diallyl) oxy triacryl zirconates,
4 and aluminozirconates having the following general structure:



5 wherein R³ is selected from the group consisting of copolymerizable alkenyl
 6 groups and carboxyfunctional substituents containing 1 or more carbon atoms.

1

1 17. The metal oxide particles of any of claims 1-16 wherein said
 2 organofunctional groups are methacryloxy aluminozirconates.

1

1 18. The metal oxide particles of any of claims 1-17 wherein one or more of the
 2 organofunctional groups and the adhesion promoters are bound to the oxide surface via an
 3 ester linkage to a phosphonate group.

1

1 19. The metal oxide particles of claim 18 wherein the phosphonate group
 2 comprises a silyl ester which may or may not comprise a polymerizable group.

1

1 20. The metal oxide particles of any of claims 1-19 wherein the mobile
 2 adhesion promoter is selected from the group consisting of silanes, phosphonates,
 3 phosphates, chelating agents, fatty acids, fatty alcohols, and ester linked fatty acids.

1 21. The metal oxide particles of any of claims 1-20 wherein the mobile
2 adhesion promoter comprises dimethyl ethoxy vinyl silane.

1

1 22. The metal oxide particles of any of claims 1-20 having an average
2 diameter of from about 10 to about 150 nanometers.

1

1 23. A composition comprising the metal oxide particles of any of claims 1-22
2 and a matrix comprising at least one monomer comprising a functionality polymerizable
3 with the organofunctional coupling agent.

1

1 24. A composite comprising the composition of claim 23 wherein said
2 functionality and said organofunctional coupling agent are copolymerized.

1

1 25. The composite of claim 24 having effective fracture toughness.

1

1 26. The composition of claim 23 comprising a dental restorative composition.

1

1 27. The composite of any of claims 24 and 25 comprising a dental restorative
2 composite.

1

1 28. The composition of claim 23 comprising a prototyping composition.

1

1 29. The composite of any of claims 24 and 25 comprising a prototyping
2 composite.

1

1 30. A method comprising:

2 providing metal oxide particles comprising a surface;

3 producing functionalized metal oxide particles by functionalizing said surface

4 with an amount of a mobile adhesion promoter and functionalizing said surface with a

5 quantity of an organofunctional coupling agent.

1

1 31. The method of claim 30 wherein the amount of the adhesion promoter is

2 effective to allow the particles to homogeneously disperse in a hydrophobic resin.

1

1 32. The method of claim 30 or 31 wherein the quantity of the organofunctional

2 coupling agent is such that, upon polymerization of said functionalized metal oxide

3 particles with polymerizable functional groups in a suitable matrix resin, the polymerized

4 compound has effective fracture toughness.

1

1 33. The method of any of claims 30-32 wherein the organofunctional coupling

2 agent also comprises an adhesion promoter.

1

1 34. The method of any of claims 30-33 wherein the metal oxide comprises a

2 metal selected from the group consisting of niobium, indium, titanium, zinc, zirconium,

3 tin, cerium, hafnium, tantalum, tungsten, bismuth, silicon and combinations thereof.

1

1 35. The method of any of claims 30-34 wherein said metal oxide comprises a
2 metal selected from the group consisting of niobium, indium, titanium, zinc, zirconium,
3 tin, cerium, hafnium, tantalum, tungsten, bismuth, and combinations thereof.

1

1 36. The method of any of claims 30-35 further comprising an alloying element
2 selected from the group consisting of aluminum, phosphorus, gallium, germanium,
3 barium, strontium, yttrium, antimony, cesium, and combinations thereof.

1

1 37. The method of any of claims 30-36 wherein said metal oxide comprises
2 zirconium oxide.

1

1 38. The method of any of claims 30-37 wherein said metal oxide comprises
2 zirconium silicate.

1

1 39. The method of any of claims 30-38 further comprising a mixture
2 comprising a matrix resin comprising monomers comprising functional groups
3 polymerizable with said organofunctional coupling agents.

1

1 40. The method of claim 30-39 comprising an average diameter effective to
2 permit curing of said mixture by photopolymerization.

1

1 41. The method of any of claims 30-40 the organofunctional coupling agent
2 comprises a polymerizable group selected from the group consisting of one or more vinyl
3 groups, acryl groups, epoxy groups, or methacryl groups.

1

1 42. The method of any of claims 30-41 wherein the organofunctional coupling
2 agent comprises a functionality selected from the group consisting of mono-, di-, and tri-
3 functional silanes, isocyanates, zirconates, aluminozirconates, zirconyl methacrylate,
4 titanates, and phosphonates.

1

1 43. The method of any of claims 30-42 wherein the organofunctional groups
2 are hydrolyzable zirconates having the following general structure:

$$3 \quad \text{R}^1\text{-O-} \text{Zr-(OR}^2\text{)}_3$$

4 wherein

5 R¹ is selected from the group consisting of hydrolyzable alkyl groups having 1 or
6 more carbon atoms; and

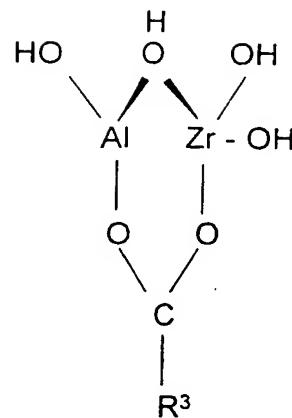
7 R² is selected from the group consisting of copolymerizable alkene substituents
8 containing 2 or more carbon atoms.

1

1 44. The method of claims 43 wherein R¹ is selected from the group consisting
2 of alkyl groups having from about 1 to about 9 carbon atoms.

1

1 45. The method of any of claims 30-44 wherein the organofunctional groups
2 comprise moieties selected from the group consisting of neopentyl (diallyl) oxy
3 trimethacryl zirconates, neopentyl (diallyl) oxy triacryl zirconates, and aluminozirconates
4 having the following general structure:



5

6 wherein R³ is selected from the group consisting of copolymerizable alkenyl
7 groups and carboxyfunctional substituents containing 1 or more carbon atoms.

1

1 46. The method of any of claims 30-45 wherein said organofunctional groups
2 are methacryloxy aluminozirconates.

1

1 47. The method of any of claims 30-46 wherein one or more of the
2 organofunctional groups and the adhesion promoters are bound to the oxide surface via an
3 ester linkage to a phosphonate group.

1

1 48. The method of any of claims 30-47 wherein the phosphonate group
2 comprises a silyl ester which may or may not comprise a polymerizable group.

1

1 49. The method of any of claims 30-48 wherein said adhesion promoter is
2 selected from the group consisting of silanes, phosphonates, phosphates, chelating agents,
3 fatty acids, fatty alcohols, and ester linked fatty acids.

1

1 50. The method of any of claims 30-49 having an average diameter of from
2 about 10 to about 150 nanometers.

1

1 51. The method of any of claims 30-50 further comprising
2 mixing said metal oxide particles with a matrix resin comprising monomers
3 comprising functional groups polymerizable with said organofunctional coupling agent,
4 forming a mixture.

1

1 52. The method of claim 51 further comprising subjecting said mixture to
2 conditions effective to cure said mixture, producing a composite.

1

1 53. A method of controlling fluidity of a mixture comprising a matrix and
2 metal oxide particles comprising a surface functionalized with an amount of an adhesion
3 promoter and with a quantity of an organofunctional coupling agent, the method
4 comprising controlling the amount of the adhesion promoter in relation to the
5 hydrophobicity of the matrix.

1

1 54. The method of any of claims 51 or 52 further comprising reducing phase
2 separation of said mixture by controlling the quantity of the organofunctional coupling
3 agent and the amount of the adhesion promoter.

1

1 55. The method of claim 54 wherein the phase separation permits uniform
2 photocuring of said mixture to a depth of about 1 millimeter or more.

1

1 56. The method of claim 55 wherein said depth is about 2 millimeters or more.

1

1 57. The method of any of claims 51-56 wherein said mixture is a dental
2 restorative material.

1

1 58 The method of any of claims 51-56 wherein said mixture is a precursor to
2 an optical device.

1

1 59. The method of any of claims 51-56 wherein said mixture is an adhesive.

1

1 60. The composition of claim 23 wherein the quantity of the organofunctional
2 coupling agent and the amount of the adhesion promoter permit uniform photocuring of
3 said mixture to a depth of about 1 millimeter or more.

1

1 61. The composition of claim 60 wherein said depth is about 2 millimeters or
2 more.

1

1 62. Optical devices comprising the metal oxide particles of any of claims 1-22.

1

1 63. A resin for making optical devices comprising the composition of claim
2 23.

1

1 64. Optical devices comprising the composite of any of claims 24-27.

1

1 65. A bone restoration comprising the composite of any of claims 24-27.

1

1 66. Metal oxide particles according to claim 1 substantially as described herein
2 in any of the examples.

1

1 67. A resin mixture according to claim 23 substantially as described herein in
2 any of the examples.

1

1 68. A composite according to any of claims 24-27 substantially as described
2 herein in any of the examples.

5

AMENDED CLAIMS

[received by the International Bureau on 30 October 2000 (30.10.00);
original claims 1 – 68 replaced by new claims 1-54 (11 pages)]

1 We claim:

2 1. Functionalized metal oxide particles comprising:
3 a surface comprising a total quantity of hydroxyl groups comprising a complexed
4 fraction comprising a reactive portion and a less reactive portion;
5 said reactive portion being complexed with a functionality selected from the group
6 consisting mobile adhesion promoters, organofunctional coupling agents,
7 and a combination thereof;
8 said less reactive portion being complexed with said mobile adhesion promoters.

1 2. The functionalized metal oxide particles of claim 1 wherein said
2 organofunctional coupling agents are irreversibly complexed with said reactive portion.

1 3. The functionalized metal oxide particles of any of claims 1 or 2 wherein at
2 least an amount of said mobile adhesion promoters are complexed with said
3 functionalities via primary chemical bonding.

1 4. The functionalized metal oxide particles of any of claims 1-3 wherein said
2 complexed fraction is about 50% or more of said total quantity.

1 5. The functionalized metal oxide particles of any of claims 1-4 wherein said
2 complexed fraction comprises substantially all of said total quantity.

1 6. The functionalized metal oxide particles of any of claims 1-5 comprising a
2 mixture further comprising a hydrophobic matrix comprising at least one monomer

3 comprising a component which is polymerizable with the organofunctional coupling
4 agent.

1

1 7. The functionalized metal oxide particles of any of claims 1-6 further
2 comprising a solvent.

1

1 8. The functionalized metal oxide particles of claim 7 wherein, upon removal
2 of said solvent from said mixture, a first composite absent said complexed fraction
3 maintains a mobile state for a first period of time, and a second composite comprising
4 said complexed fraction maintains a mobile state for a second period of time longer than
5 said first period of time.

1

1 9. The functionalized metal oxide particles of claims 1-7 wherein the
2 organofunctional coupling agent also comprises an adhesion promoter.

1

1 10. The functionalized metal oxide particles of any of claims 1-9 wherein the
2 metal oxide comprises a metal selected from the group consisting of niobium, indium,
3 titanium, zinc, zirconium, tin, cerium, hafnium, tantalum, tungsten, bismuth and
4 combinations thereof.

1

1 11. The functionalized metal oxide particles of any of claims 1-9 wherein said
2 metal oxide comprises silicon.

1

1 12. The functionalized metal oxide particles of any of claims 10-11 further
2 comprising an alloying element selected from the group consisting of aluminum,
3 phosphorus, gallium, germanium, barium, strontium, yttrium, niobium, antimony, cesium,
4 and combinations thereof.

1

1 13. The functionalized metal oxide particles of any of claims 1-12 wherein
2 said metal comprises zirconium.

1

1 14. The functionalized metal oxide particles of any of claims 1-13 comprising
2 an average diameter effective to permit curing of said mixture by photopolymerization.

1

1 15. The functionalized metal oxide particles of any of claims 1-14 wherein
2 said complexed fraction is effective to disperse said functionalized metal oxide particles
3 in a hydrophobic resin.

1

1 16. The functionalized metal oxide particles of any of claims 1-15 wherein the
2 organofunctional coupling agent comprises a polymerizable group selected from the
3 group consisting of one or more vinyl groups, acryl groups, epoxy groups, or methacryl
4 groups.

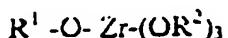
1

1 17. The functionalized metal oxide particles of any of claims 1-16 wherein the
2 organofunctional coupling agent comprises a functionality selected from the group
3 consisting of mono-, di-, and tri-functional silanes, isocyanates, zirconates,
4 aluminozirconates, zirconyl methacrylate, titanates, and phosphonates.

1

1 18. The functionalized metal oxide particles of any of claims 2-17 wherein the
2 organofunctional groups are hydrolyzable zirconates having the following general
3 structure:

4



5 wherein

6 R¹ is selected from the group consisting of hydrolyzable alkyl groups and
7 hydrolyzable alkenyl groups having 1 or more carbon atoms; and

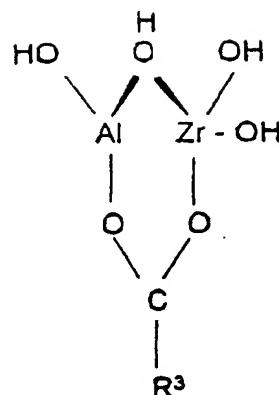
8 R² is selected from the group consisting of copolymerizable alkenyl substituents
9 containing 2 or more carbon atoms.

1

1 19. The functionalized metal oxide particles of claim 18 wherein R¹ is selected
2 from the group consisting of alkyl groups having from about 1 to about 9 carbon atoms.

1

1 20. The functionalized metal oxide particles of claim 19 wherein the
2 organofunctional groups comprise moieties selected from the group consisting of
3 neopentyl (diallyl) oxy trimethacryl zirconates, neopentyl (diallyl) oxy triacryl zirconates,
4 and aluminozirconates having the following general structure:



5 wherein R³ is selected from the group consisting of copolymerizable alkenyl
 6 groups and carboxyfunctional substituents containing 1 or more carbon atoms.

1
 1 21. The functionalized metal oxide particles of any of claims 2-20 wherein
 2 said organofunctional groups are methacryloxy aluminozirconates.

1
 1 22. The functionalized metal oxide particles of any of claims 1-21 wherein one
 2 or more of a functionality selected from the group consisting of said organofunctional
 3 groups and said mobile adhesion promoter is bound to the oxide surface via an ester
 4 linkage to a phosphonate group.

1
 1 23. The functionalized metal oxide particles of claim 22 wherein the
 2 phosphonate group comprises a silyl ester which may or may not comprise a
 3 polymerizable group.

1
 1 24. The functionalized metal oxide particles of any of claims 1-23 wherein
 2 said mobile adhesion promoter is selected from the group consisting of silanes,

3 phosphonates, phosphates, chelating agents, fatty acids, fatty alcohols, and ester linked
4 fatty acids.

1
1 25. The functionalized metal oxide particles of any of claims 1-24 wherein
2 said mobile adhesion promoter comprises dimethyl ethoxy vinyl silane.

1
1 26. The functionalized metal oxide particles of any of claims 1-25 having an
2 average diameter of from about 10 to about 150 nanometers.

1
1 27. The composite comprising the composition of any of claims 6-26 wherein
2 said component and said organofunctional coupling agent are copolymerized.

1
1 28. The composite of claim 27 comprising a dental restorative composition.

1
1 29. The composite of claim 27 comprising a prototyping composition.

1
1 30. A method for producing functionalized metal oxide particles comprising:
2 providing metal oxide particles comprising a surface comprising a total quantity
3 of hydroxyl groups comprising a reactive portion and a less reactive
4 portion;
5 forming first complexes between said reactive portion and a functionality selected
6 from the group consisting mobile adhesion promoters, organofunctional
7 coupling agents, and a combination thereof; and,

8 forming second complexes between said less reactive portion and said mobile
9 adhesion promoters;
10 said first complexes and said second complexes comprising a complexed fraction.

1 31. The method of claim 30 further comprising mixing said functionalized
2 metal oxide particles in a solvent with a hydrophobic matrix, forming mixture comprising
3 at least one monomer comprising a component polymerizable with the organofunctional
4 coupling agent.

1 32. The method of claim 31 wherein, upon removal of said solvent from said
2 mixture, a first composite absent said complexed fraction maintains a mobile state for a
3 first period of time, and a second composite comprising said complexed fraction
4 maintains a mobile state for a second period of time longer than said first period of time.

5 33. The method of any of claims 30-32 wherein at least a portion of said first
6 complexes comprise organofunctional coupling agents irreversibly complexed with said
7 reactive portion.

1 34. The method of any of claims 30-34 wherein at least an amount of said
2 second complexes comprise said mobile adhesion promoters bound to said functionalities
3 via primary chemical bonding.

1 35. The method of any of claims 30-34 wherein said complexed fraction is
2 about 50% or more of said total quantity.

1

1 36. The method of any of claims 30-35 wherein said complexed fraction
2 comprises substantially all of said total quantity.

1

1 37. The method of claims 30-36 wherein the organofunctional coupling agent
2 also comprises an adhesion promoter.

1

1 38. The functionalized metal oxide particles of any of claims 30-37 wherein
2 the metal oxide comprises a metal selected from the group consisting of niobium,
3 indium, titanium, zinc, zirconium, tin, cerium, hafnium, tantalum, tungsten, bismuth and
4 combinations thereof.

1

1 39. The functionalized metal oxide particles of any of claims 30-38 wherein
2 said metal oxide comprises silicon.

1

1 40. The method of any of claims 30-39 further comprising an alloying element
2 selected from the group consisting of aluminum, phosphorus, gallium, germanium,
3 barium, strontium, yttrium, niobium, antimony, cesium, and combinations thereof.

1

1 41. The method of any of claims 30-40 wherein said metal comprises
2 zirconium.

1

1 42. The method of any of claims 30-41 comprising effectively curing said
2 mixture by photopolymerization.

1

1 43. The method of any of claims 30-42 wherein the organofunctional coupling
2 agent comprises a polymerizable group selected from the group consisting of one or
3 more vinyl groups, acryl groups, epoxy groups, or methacryl groups.

1

1 44. The method of any of claims 30-43 wherein the organofunctional coupling
2 agent comprises a functionality selected from the group consisting of mono-, di-, and tri-
3 functional silanes, isocyanates, zirconates, aluminozirconates, zirconyl methacrylate,
4 titanates, and phosphonates.

1

1 45. The functionalized metal oxide particles of any of claims 30-44 wherein
2 the organofunctional groups are hydrolyzable zirconates having the following general
3 structure:

4

wherein

6

R^1 is selected from the group consisting of hydrolyzable alkyl groups and hydrolyzable alkenyl groups having 1 or more carbon atoms; and

1

8

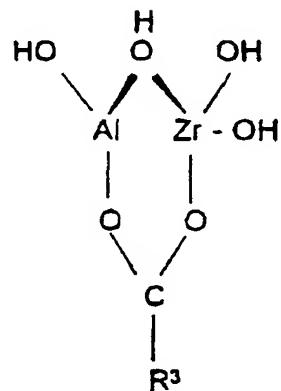
containing 2 or more carbon atoms.

1

1

2

1 47. The method of any of claims 30-46 wherein the organofunctional groups
 2 comprise moieties selected from the group consisting of neopentyl (diallyl) oxy
 3 trimethacryl zirconates, neopentyl (diallyl) oxy triacryl zirconates, and aluminozirconates
 4 having the following general structure:



5 wherein R³ is selected from the group consisting of copolymerizable alkenyl
 6 groups and carboxyfunctional substituents containing 1 or more carbon atoms.

1 48. The method of any of claims 30-47 wherein said organofunctional groups
 2 are methacryloxy aluminozirconates.

1 49. The method of any of claims 30-48 wherein one or more of a complex
 2 selected from the group consisting of said first complexes to an organofunctional group
 3 and said second complexes comprise an ester linkage to a phosphonate group.

1 50. The method of claim 30-49 wherein the phosphonate group comprises a
 2 silyl ester which may or may not comprise a polymerizable group.

1 51. The method of any of claims 30-50 wherein said mobile adhesion
2 promoter is selected from the group consisting of silanes, phosphonates, phosphates,
3 chelating agents, fatty acids, fatty alcohols, and ester linked fatty acids.

1

1 52. The method of any of claims 30-51 wherein said mobile adhesion
2 promoter comprises dimethyl ethoxy vinyl silane.

1

1 53. The method of claim 42 wherein said curing produces a dental restorative
2 composition.

1

1 54. The method of claim 42 wherein said curing produces a prototyping
2 composition.

INTERNATIONAL SEARCH REPORT

Intern	Application No
PCT/US 00/13708	

A. CLASSIFICATION OF SUBJECT MATTER					
IPC 7	A61K6/06	A61K6/083	A61L27/44	C09C1/00	C09C3/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61L C09C

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, PAJ, WPI Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 722 992 A (DEGUSSA) 24 July 1996 (1996-07-24) abstract; claim 1	1,2
X	WO 94 16129 A (PPG INDUSTRIES INC) 21 July 1994 (1994-07-21) abstract; claims 1-4	1,2
X	WO 92 16183 A (THERA GES FUER PATENTE) 1 October 1992 (1992-10-01)	1-6, 8-12, 30-42, 47-62
A	the whole document	18-29
	—	—/—

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

24 August 2000

Date of mailing of the international search report

31/08/2000

Name and mailing address of the ISA
European Patent Office, P.B. 5818 Patentiaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl.
Fax: (+31-70) 340-3016

Authorized officer

Siebel, E

INTERNATIONAL SEARCH REPORT

Intern:	Application No
PCT/US	00/13708

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 99 17716 A (DENTSPLY INT INC) 15 April 1999 (1999-04-15) page 4, line 10 -page 10, line 23; claims 1-20 —	1-27
A	US 4 539 048 A (COHEN LAWRENCE B) 3 September 1985 (1985-09-03) cited in the application the whole document —	1-8, 10-23, 30-49
A	US 4 623 738 A (SUGERMAN GERALD ET AL) 18 November 1986 (1986-11-18) cited in the application column 1, line 13 -column 6, line 55; claims 1-18 —	12-15

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern: Application No

PCT/US 00/13708

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
EP 0722992	A 24-07-1996	DE 19500674 A FR 2729380 A GB 2296915 A,B JP 8253321 A US 6022404 A		18-07-1996 19-07-1996 17-07-1996 01-10-1996 08-02-2000
WO 9416129	A 21-07-1994	NONE		
WO 9216183	A 01-10-1992	DE 9103321 U AT 126693 T DE 59203367 D EP 0531483 A ES 2079187 T US 5401528 A		27-08-1992 15-09-1995 28-09-1995 17-03-1993 01-01-1996 28-03-1995
WO 9917716	A 15-04-1999	AU 9393898 A BR 9806297 A EP 0969789 A		27-04-1999 14-03-2000 12-01-2000
US 4539048	A 03-09-1985	AT 50998 T AU 581843 B AU 2577684 A CA 1301182 A DE 3481618 D EP 0135566 A IT 1210129 B JP 7059588 B JP 60500537 T NZ 207068 A WO 8403093 A US 4539049 A		15-03-1990 09-03-1989 30-08-1984 19-05-1992 19-04-1990 03-04-1985 06-09-1989 28-06-1995 18-04-1985 29-04-1988 16-08-1984 03-09-1985
US 4623738	A 18-11-1986	AU 575165 B AU 4247585 A CA 1237140 A CN 1005712 B DE 3579194 D EP 0164227 A IN 170651 A IN 170585 A JP 2115521 C JP 5339421 A JP 8034745 B JP 1875876 C JP 2138285 A JP 6000791 B KR 9102535 B MX 164160 B NO 851845 A,B, US 4657988 A		21-07-1988 21-11-1985 24-05-1988 08-11-1989 20-09-1990 11-12-1985 02-05-1992 18-04-1992 06-12-1996 21-12-1993 29-03-1996 07-10-1994 28-05-1990 05-01-1994 23-04-1991 20-07-1992 15-11-1985 14-04-1987